WEST Search History

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DATE: Friday, September 24, 2004

Hide?	Set Name	Query	Hit Count
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☐	L13	L12 and enzyme	14
☐	L12	L8 and aspartic	14
☐	L11	L8 and aspartic enzyme	0
☐	L10	L9 and aspart? enzyme	0
☐	L9	L8 and cancer	15
☐	L8	L6 and inhibit?	15
☐	L7	L6 with inhibit?	0
☐	L6	cathepsin D precursor	27
☐	L5	L1 and metastatis	0
☐	L4	L1 and cancer	1
☐	L3	L1 and treat cancer	0
☐	L2	L1 and protein fragments	1
☐	L1	aspartic enzyme	14

END OF SEARCH HISTORY

=> d ibib hitseq abs tot

L2 ANSWER 1 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:241459 HCAPLUS
DOCUMENT NUMBER: 132:275964
TITLE: Novel human aspartase homologous to cathepsin D precursor and use for producing anti-metastasis plasma protein fragments
INVENTOR(S): Morikawa, Wataru; Kaminaka, Kazuyoshi; Takemoto, Sumiyo; Maeda, Hiroaki; Nozaki, Chikateru; Miyamoto, Seiji
PATENT ASSIGNEE(S): Juridical Foundation the Chemo-Sero-Therapeutic Research Institute, Japan
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000020570	A1	20000413	WO 1999-JP5322	19990929
W: US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
JP 2000106882	A2	20000418	JP 1998-296095	19981002
EP 1118660	A1	20010725	EP 1999-970118	19990929
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

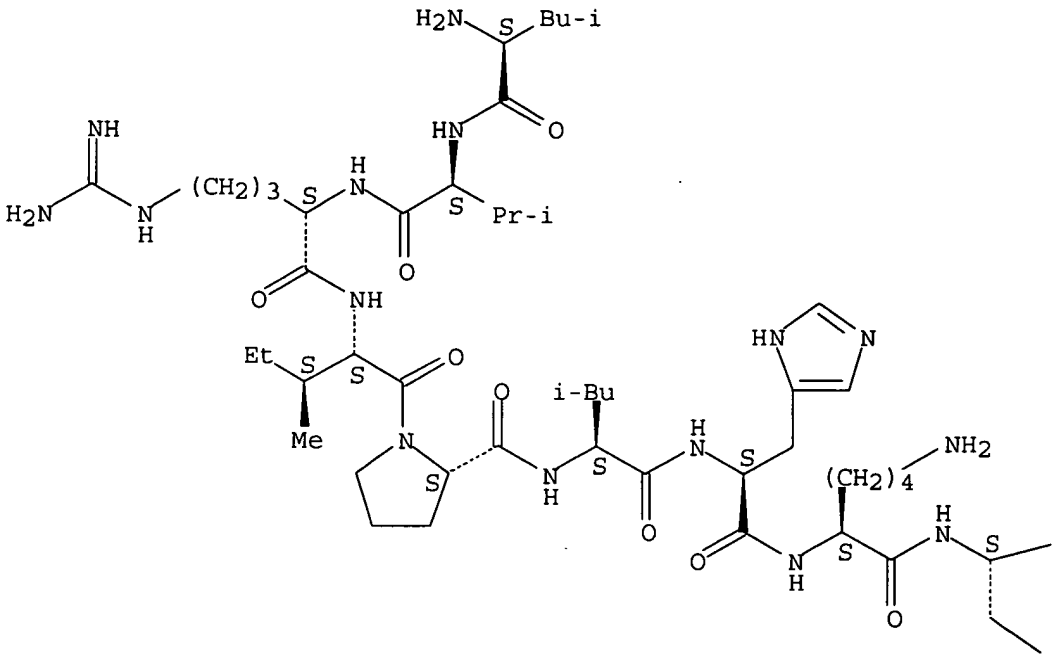
PRIORITY APPLN. INFO.: JP 1998-296095 A 19981002
WO 1999-JP5322 W 19990929

IT **254754-41-1**
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(N-terminus of human aspartase PACE4 (plasminogen angiostatin converting enzyme of pH 4); novel human aspartase homologous to cathepsin D precursor and use for producing anti-metastasis plasma protein fragments)
RN 254754-41-1 HCAPLUS
CN L-Threonine, L-leucyl-L-valyl-L-arginyl-L-isoleucyl-L-prolyl-L-leucyl-L-histidyl-L-lysyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

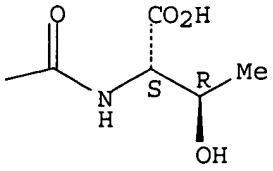
SEQ 1 LVRIPLHKFT

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 2-A

Ph

AB A novel aspartase, PACE4 (plasminogen angiostatin converting enzyme of pH 4), is prepared from cell line PC-3 that was established from human prostate cancer and characterized. PACE4 exhibits a mol. weight of 45 kDa as determined by non-reducing SDS-PAGE and LVRIPLHKFT at the N-terminus. PACE4 aspartase is highly homol. to human cathepsin D precursor and can degrade plasma proteins such as plasminogen, fibronectin, vitronectin, and human hepatic growth factor into fragments that have the angiostatin-like activities and thus the anti-metastasis effects. A pharmaceutical composition containing PACE4 for the prevention of treatment of solid cancers, diabetic retinopathy, or rheumatism is also claimed.

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 2 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1999:458339 HCAPLUS

DOCUMENT NUMBER: 132:91503

TITLE: Modulation of Proliferation and Chemosensitivity by Procathepsin D and Its Peptides in Ovarian Cancer

AUTHOR(S): Bazzett, Lisa B.; Watkins, Christopher S.; Gercel-Taylor, Cicek; Taylor, Douglas D.

CORPORATE SOURCE: Departments of Obstetrics & Gynecology, University of Louisville School of Medicine, Louisville, KY, 40292, USA

SOURCE: Gynecologic Oncology (1999), 74(2), 181-187
CODEN: GYNOA3; ISSN: 0090-8258

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

IT **254754-41-1P**
RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
(Peptide 1, amino acids 21 to 30 of procathepsin D; modulation of proliferation and chemosensitivity by procathepsin D and peptides in human ovarian cancer)

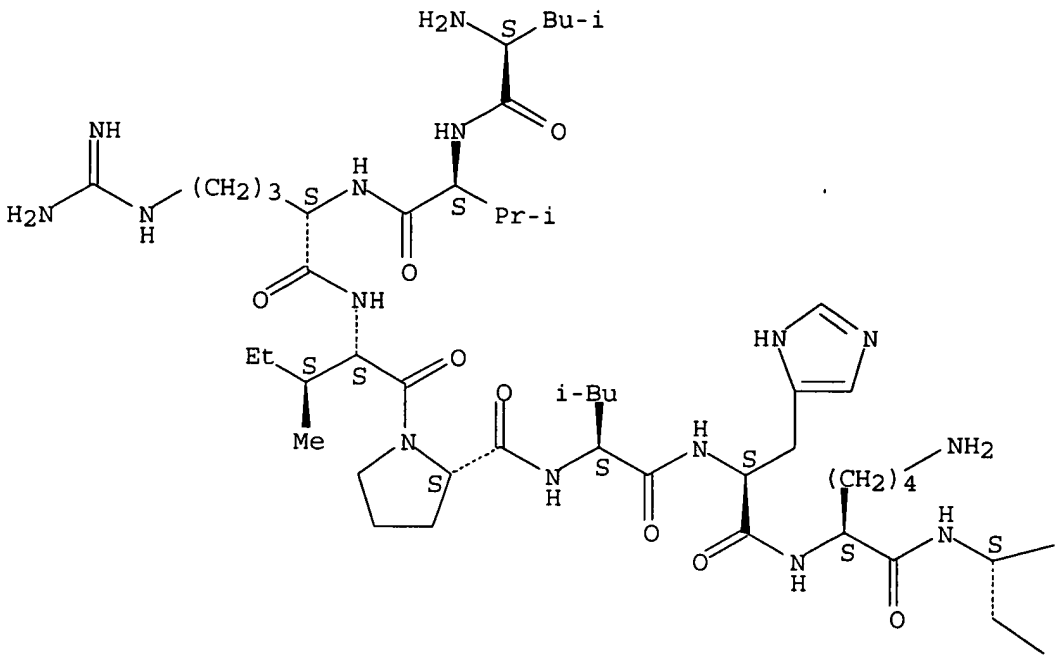
RN 254754-41-1 HCAPLUS

CN L-Threonine, L-leucyl-L-valyl-L-arginyl-L-isoleucyl-L-prolyl-L-leucyl-L-histidyl-L-lysyl-L-phenylalanyl- (9CI) (CA INDEX NAME)

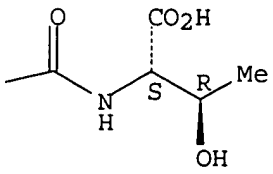
SEQ 1 LVRIPLHKFT

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B



PAGE 2-A

Ph

AB Since the presence of precursors (pro-forms) of the aspartyl endoprotease, cathepsin D, appears to be linked with tumor progression, their presence was examined in sera and tumor tissues of ovarian cancer patients. The role of cathepsin D pro-forms was further assessed in the dysregulated proliferation and chemoresistance observed in advanced ovarian cancer. Cathepsin D was isolated from sera of ovarian cancer patients (n = 20) and normal volunteers (n = 11), as well as from solubilized normal ovarian epithelium (n = 8) and ovarian epithelial tumor tissue (n = 12). The specific mol. forms of cathepsin D were analyzed in these samples by Western immunoblot. Multiple circulating mol. weight forms of cathepsin D were identified in ovarian cancer patients ranging from 24 to 60 kDa, while in normal controls, a major band was observed at 34 kDa in all samples and minor bands corresponding to 27 and 48 kDa were detected in approx. half of the controls. To assess its consequences on ovarian cancer, the 52-kDa protein was immunopptd. from culture medium of an exponentially growing ovarian tumor cell line and was further purified by reverse-phase high-pressure liquid chromatog. Its effect on proliferation was assayed by determining cell doubling times and their chemosensitivity was measured in a standard cytotoxicity assay using cisplatin. In addition, decapeptides corresponding to the pro-portion of cathepsin D were analyzed in parallel. Procathepsin D and one decapeptide, peptide 2, as well as IGF-II (as a known pos.) increased cell proliferation, with doubling times of 28.4, 28.8, and 30.3 h, resp., vs. untreated UL-1 cells (36.4 h). Procathepsin D treatment of UL-1 tumor cells significantly increased the cisplatin LD50 (74.9 μg/mL) over untreated (33.9 μg/mL) as well as IGF-II-treated (38.8 μg/mL) cells. Peptide 2 also showed a significant increase in LD50 (69.5 μg/mL) compared to untreated and peptide 1-treated cells (37.1 μg/mL). There are several unique forms of cathepsin D expressed and accumulated by ovarian tumors and these forms are detectable in the sera of those with ovarian cancer. The presence of these procathepsin D can increase the proliferation of these tumor cells, while decreasing their sensitivity to chemotherapeutic agents. While procathepsin D and IGF-II both enhance proliferation, only procathepsin D (and peptide 2) appears to modulate chemosensitivity, suggesting a sep. receptor or pathway for this consequence. (c) 1999 Academic Press.

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:582912 HCAPLUS
DOCUMENT NUMBER: 129:211700
TITLE: Method for inhibition of breast tumor growth by inhibition of procathepsin D activation peptide
INVENTOR(S): Fusek, Martin; Vetvicka, Vaclav
PATENT ASSIGNEE(S): Oklahoma Medical Research Foundation, USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5800814	A	19980901	US 1994-232997	19940422
PRIORITY APPLN. INFO.:			US 1994-232997	19940422

IT **212325-21-8**
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(procathepsin D activation peptide inhibition for inhibition of breast tumor growth)
RN 212325-21-8 HCAPLUS
CN Glycine, L-leucyl-L-valyl-L-arginyl-L-isoleucyl-L-prolyl-L-leucyl-L-histidyl-L-lysyl-L-phenylalanyl-L-threonyl-L-seryl-L-isoleucyl-L-arginyl-L-arginyl-L-threonyl-L-methionyl-L-seryl-L-α-glutamyl-L-valylglycylglycyl-L-seryl-L-valyl-L-α-glutamyl-L-α-aspartyl-L-leucyl-L-isoleucyl-L-alanyl-L-lysylglycyl-L-prolyl-L-valyl-L-seryl-L-lysyl-L-tyrosyl-L-seryl-L-glutaminyl-L-alanyl-L-prolyl-L-alanyl-L-valyl-L-threonyl-L-α-glutamyl- (9CI) (CA INDEX NAME)

SEQ 1 LVRIPLHKFT SIRRTMSEVG GSVEDLIAKG PVSKYSQAPA VTEG

AB Human procathepsin D was demonstrated to be mitogenic for breast cancer cells but not normal cells. The activation peptide of the procathepsin D appears to be responsible, since inhibition of enhancement of proliferation of breast cancer cells can be obtained by inhibition of the activation peptide through the use of an agent such as an antibody immunoreactive with the activation peptide.
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 4 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:536377 HCAPLUS
DOCUMENT NUMBER: 103:136377
TITLE: Cloning and sequence analysis of cDNA for human cathepsin D
AUTHOR(S): Faust, Phyllis L.; Kornfeld, Stuart; Chirgwin, John M.
CORPORATE SOURCE: Sch. Med., Washington Univ., St. Louis, MO, 63110, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1985), 82(15), 4910-14
CODEN: PNASA6; ISSN: 0027-8424
DOCUMENT TYPE: Journal
LANGUAGE: English
IT **98443-40-4**
RL: PRP (Properties)
(amino acid sequence of)
RN 98443-40-4 HCAPLUS
CN Cathepsin D, pro- (human clone pHKCD45 protein moiety reduced) (9CI) (CA INDEX NAME)

SEQ
1 LVRIPLHKFT SIRRTMSEVG GSVEDLIAKG PVSKVSQAVP AVTEGPIPEV
51 LKNYMDAQYY GEIGIGTPPQ CFTVVFDTGS SNLWVPSIHC KLLDIACWIH
101 HKVNSDKSST VVKNGTSFDI HVGSGSLSGV LSQDTVSVPC QSASSASALG
151 GVKVERQVFG EATKQPGITF IAAKFDGILG MAVPRISVNN VLPVFDNLMQ
201 QKLVDQNIFS FVLSRDPDAQ PGGELMLGGT DSKVVKGSLS VLNVTRKAVW
251 QVHLDQVEVA SGLTLCKEGC EAIVDTGTSL MVGPVDEVRE LQKAIGAVPL
301 IQGEYMIPCE KVSTLPAITL KLGGKGYKLS PEDYTLKVSQ AGKTLCLSGF
351 MGMDIPPPSG PLWILGDVFI GRYYTVFDRD NNRVGFAEAA RL

AB An 1110-base-pair cDNA clone for human cathepsin D was obtained by screening a λgt10 human hepatoma G2 cDNA library with a human renin exon 3 genomic fragment. Poly(A)+ RNA blot anal. with this cathepsin D

clone demonstrated a message length of .apprx.2.2 kilobases. The partial clone was used to screen a size-selected human kidney cDNA library, from which 2 cathepsin D recombinant plasmids with inserts of ≈2200 and 2150 base pairs were obtained. The nucleotide sequences of these clones and of the λgt10 clone were determined The amino acid sequence predicted from the cDNA sequence shows that human cathepsin D consists of 412 amino acids with 20 and 44 amino acids in a pre- and a prosegment, resp. The mature protein region shows 87% amino acid identity with porcine cathepsin D but differs in having 9 addnl. amino acids. Two of these are at the terminus; the other 7 are positioned between the previously determined junction for the light and heavy chains of porcine cathepsin D. A high degree of sequence homol. was observed between human cathepsin D and other aspartyl proteases, suggesting a conservation of 3-dimensional structure in this family of proteins.

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DIALOG INFORMATION SERVICES
PLEASE LOGON:
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ENTER PASSWORD:
 ******** HHHHHHHH SSSSSSSS?  ********
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Dialog level 05.02.01D

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Logon file405 10may05 07:01:17
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***German Patents Fulltext (File 324)

***Beilstein Abstracts (File 393)
***Beilstein Facts (File 390)
***Beilstein Reactions (File 391)
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RELOADED
***Medline (Files 154 & 155)
***ToxFile (File 156)

RESUMED UPDATING
***Canadian Business and Current Affairs (262)
***CorpTech (559)
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REMOVED

***Health News Daily (43)
***FDC Reports Gold Sheet/Silver Sheet (184)
***FDC Reports (186/187)
***NDA Pipeline: New Drugs (189)
                     ***
     >>> Enter BEGIN HOMEBASE for Dialog Announcements <<<
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KWIC is set to 50.
HILIGHT set on as '*'
PICKS is set ON as an alias for
5,159,143,358,340,344,348,447,73,155,349,266,10,34,434,42,43,50,65,71,91,94,14
4,198,304,370,467,444,357,156,157.
* * *
SYSTEM:HOME
Cost is in DialUnits
Menu System II: D2 version 1.7.9 term=ASCII
                      *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
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  5.  Product Descriptions

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  6.  DIALOG(R) Document Delivery
  7.  Data Star(R)

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 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
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Terminal set to DLINK
                    *** DIALOG HOMEBASE(SM) Main Menu ***

 Information:
  1.  Announcements (new files, reloads, etc.)
  2.  Database, Rates, & Command Descriptions
  3.  Help in Choosing Databases for Your Topic
  4.  Customer Services (telephone assistance, training, seminars, etc.)
  5.  Product Descriptions

 Connections:
  6.  DIALOG(R) Document Delivery
  7.  Data Star(R)

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      /H = Help            /L = Logoff          /NOMENU = Command Mode


Enter an option number to view information or to connect to an online
 service.  Enter a BEGIN command plus a file number to search a database
(e.g., B1 for ERIC).
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  File   5:Biosis Previews(R) 1969-2005/May W1
         (c) 2005 BIOSIS
  File 159:Cancerlit 1975-2002/Oct
         (c) format only 2002 Dialog Corporation
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  File 143:Biol. & Agric. Index 1983-2005/Apr
         (c) 2005 The HW Wilson Co
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File 358:Current BioTech Abs 1983-2005/Apr
(c) 2005 DECHEMA
File 340:CLAIMS(R)/US Patent 1950-05/May 05
(c) 2005 IFI/CLAIMS(R)
***File 340: 2004 Reload is online as of October 6, 2004. Pricing** changes effective October 1, 2004. See HELP NEWS 340 for details.
File 344:Chinese Patents Abs Aug 1985-2004/May
(c) 2004 European Patent Office
File 348:EUROPEAN PATENTS 1978-2005/May W01
(c) 2005 European Patent Office
File 447:IMS Patent Focus 2005/Apr
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(c) 2005 Elsevier Science B.V.
File 155:MEDLINE(R) 1951-2005/May W2
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Comp & dist by NTIS, Intl Copyright All Rights Res
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File 34:SciSearch(R) Cited Ref Sci 1990-2005/May W1
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(c) 2005 Elsevier Science B.V.
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2001 (c) Action Potential
File 94:JICST-EPlus 1985-2005/Mar W3
(c)2005 Japan Science and Tech Corp(JST)
File 144:Pascal 1973-2005/May W1
(c) 2005 INIST/CNRS
File 198:Health Devices Alerts(R) 1977-2005/Feb W2
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File 304:The Merck Index Online(SM) 2004/S2
(c) 2004 MERCK & CO. INC.
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File 370:Science 1996-1999/Jul W3
(c) 1999 AAAS
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File 467:ExtraMED(tm) 2000/Dec
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***File 467: F467 no longer updates; see Help News467.**
File 444:New England Journal of Med. 1985-2005/Apr W4
(c) 2005 Mass. Med. Soc.
File 357:Derwent Biotech Res. _1982-2005/May W2
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File 156:ToxFile 1965-2005/May W1
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File 157:BIOSIS Toxicology (c) 2004 BIOSIS

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S2 15 RD (unique items)
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2/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0014822064 BIOSIS NO.: 200400189750
Structure-based approaches to the development of novel anti-malarials.
AUTHOR: Brady R Leo (Reprint); Cameron Angus
AUTHOR ADDRESS: Department of Biochemistry, University of Bristol, Bristol, BS9 3TD, UK**UK
AUTHOR E-MAIL ADDRESS: L.Brady@bris.ac.uk
JOURNAL: Current Drug Targets 5 (2): p137-149 February 2004 2004
MEDIUM: print
ISSN: 1389-4501 _(ISSN print)
DOCUMENT TYPE: Article; Literature Review
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 210756-42-6: 1-deoxy-D-xylulose 5-phosphate reductoisomerase; 9024-52-6: aldolase; 220247-45-0: *aspartic acid proteases*; 37353-41-6: cysteine proteases; 165587-69-9: cysteine proteases; 9002-03-3: dihydrofolate reductase; 9001-50-7Q: glyceraldehyde 3-phosphate dehydrogenase; 9028-92-6Q: glyceraldehyde 3-phosphate dehydrogenase; 37250-87-6Q: glyceraldehyde 3-phosphate dehydrogenase; 162995-20-2Q: glyceraldehyde 3-phosphate dehydrogenase; 9001-50-7: glyceraldehyde 3-phosphate dehydrogenase; 14875-96-8: heme; 9001-60-9: lactate dehydrogenase; 81669-70-7: metalloproteinase; 369636-51-1: peptide deformylase; 9023-78-3: triosephosphate isomerase
ENZYME COMMISSION NUMBER: EC 1.1.1.267: 1-deoxy-D-xylulose 5-phosphate reductoisomerase; EC 4.1.2.13: aldolase; EC 1.5.1.3: dihydrofolate reductase; EC 1.2.1.12: glyceraldehyde 3-phosphate dehydrogenase; EC 1.1.1.27: lactate dehydrogenase; EC 3.4.24.21: metalloproteinase; EC 3.5.1.88: peptide deformylase; EC 5.3.1.1: triosephosphate isomerase
DESCRIPTORS:
MAJOR CONCEPTS: Enzymology--Biochemistry and Molecular Biophysics; Methods and Techniques; Parasitology; Pharmacology
BIOSYSTEMATIC NAMES: Hominidae--Primates, Mammalia, Vertebrata, Chordata, Animalia; Sporozoa--Protozoa, Invertebrata, Animalia
ORGANISMS: human (Hominidae)--host; Plasmodium falciparum (Sporozoa)--

parasite
ORGANISMS: PARTS ETC: food vacuole
COMMON TAXONOMIC TERMS: Chordates; Humans; Mammals; Primates; Vertebrates ; Animals; Invertebrates; Microorganisms; Protozoans
DISEASES: malaria--blood and lymphatic disease, parasitic disease, drug therapy
MESH TERMS: Malaria (MeSH)
CHEMICALS & BIOCHEMICALS: 1-deoxy-D-xylulose 5-phosphate reductoisomerase; aldolase; *aspartic acid proteases *{plasmepsins}--drug target; cysteine proteases {falcipains}--drug target; dihydrofolate reductase; drug-enzyme complexes; enoyl reductase; glyceraldehyde 3-phosphate dehydrogenase; heme--degradation; isoprenoid synthesis inhibitors--antiinfective-drug, antiparasitic-drug, antiprotozoal-drug; lactate dehydrogenase; metabolic enzymes; metalloproteinase; novel anti-malarials--antiinfective-drug, antiparasitic-drug, antiprotozoal-drug, development; peptide deformylase; purine salvage inhibitors--antiinfective-drug, antiparasitic-drug, antiprotozoal-drug; triosephosphate isomerase
METHODS & EQUIPMENT: protein crystallography--crystallographic techniques , laboratory techniques
MISCELLANEOUS TERMS: fatty acid biosynthesis pathway; glycolytic pathway; inhibitor-protein contacts--improvement, visualization; protein prenylation; structure-based approaches; Literature Review
CONCEPT CODES:
10065 Biochemistry studies - Porphyrins and bile pigments
10802 Enzymes - General and comparative studies: coenzymes
12512 Pathology - Therapy
15006 Blood - Blood, lymphatic and reticuloendothelial pathologies
22002 Pharmacology - General
22005 Pharmacology - Clinical pharmacology
25502 Development and Embryology - General and descriptive
38502 Chemotherapy - General, methods and metabolism
38510 Chemotherapy - Antiparasitic agents
60502 Parasitology - General
60504 Parasitology - Medical
64002 Invertebrata: comparative, experimental morphology, physiology and pathology - Protozoa
BIOSYSTEMATIC CODES:
86215 Hominidae
35400 Sporozoa

2/9/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013917457 BIOSIS NO.: 200200510968
Investigating the substrate specificity of HTLV-I protease
AUTHOR: Mariani Victoria (Reprint); Herger Bryan (Reprint); Shuker Suzanne B
AUTHOR ADDRESS: Department of Chemistry, Georgia Institute of Technology, Petite Institute for Bioengineering and Bioscience, 315 Ferst Dr, Atlanta, GA, 30324, USA**USA
JOURNAL: Abstracts of Papers American Chemical Society 224 (1-2): pMEDI 204 2002 2002
MEDIUM: print
CONFERENCE/MEETING: 224th National Meeting of the American Chemical Society Boston, MA, USA August 18-22, 2002; 20020818
ISSN: 0065-7727

DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
DESCRIPTORS:
MAJOR CONCEPTS: Enzymology--Biochemistry and Molecular Biophysics; Infection; Pharmacology
BIOSYSTEMATIC NAMES: Retroviridae--DNA and RNA Reverse Transcribing Viruses, Viruses, Microorganisms
ORGANISMS: human T lymphotropic virus type 1 (Retroviridae)--pathogen
COMMON TAXONOMIC TERMS: DNA and RNA Reverse Transcribing Viruses; Microorganisms; Viruses
CHEMICALS & BIOCHEMICALS: *aspartic acid protease*; enzyme inhibitor drugs
MISCELLANEOUS TERMS: drug discovery; Meeting Abstract; Meeting Abstract
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
10802 Enzymes - General and comparative studies: coenzymes
12512 Pathology - Therapy
22002 Pharmacology - General
33506 Virology - Animal host viruses
36006 Medical and clinical microbiology - Virology
BIOSYSTEMATIC CODES:
03305 Retroviridae

2/9/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0013653988 BIOSIS NO.: 200200247499
Endosomal proteolysis of internalized insulin at the C-terminal region of the B chain by cathepsin D
AUTHOR: Authier Francois (Reprint); Metioui Mourad; Fabrega Sylvie; Kouach Mostafa; Briand Gilbert
AUTHOR ADDRESS: Faculte de Pharmacie Paris XI, INSERM U510, 5 Rue Jean-Baptiste Clement, 92296, Chatenay-Malabry, France**France
JOURNAL: Journal of Biological Chemistry 277 (11): p9437-9446 March 15, 2002 2002
MEDIUM: print
ISSN: 0021-9258
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The endosomal compartment of hepatic parenchymal cells contains an acidic endopeptidase, endosomal acidic insulinase, which hydrolyzes internalized insulin and generates the major primary end product A1-21-B1-24 insulin resulting from a major cleavage at residues PheB24-PheB25. This study addresses the nature of the relevant endopeptidase activity in rat liver that is responsible for most receptor-mediated insulin degradation in vivo. The endosomal activity was shown to be aspartic acid protease cathepsin D (CD), based on biochemical similarities to purified CD in 1) the rate and site of substrate cleavage, 2) pH optimum, 3) sensitivity to pepstatin A, and 4) binding to pepstatin A-agarose. The identity of the protease was immunologically confirmed by removal of greater than 90% of the insulin-degrading activity associated with an endosomal lysate using polyclonal antibodies to CD. Moreover, the elution profile of the endosomal acidic insulinase activity on a gel-filtration TSK-GEL G3000 SWXL high performance liquid

chromatography column corresponded exactly with the elution profile of the immunoreactive 45-kDa mature form of endosomal CD. Using nondenaturating immunoprecipitation and immunoblotting procedures, other endosomal aspartic acid proteases such as cathepsin E and beta-site amyloid precursor protein-cleaving enzyme (BACE) were ruled out as candidate enzymes for the endosomal degradation of internalized insulin. Immunofluorescence studies showed a largely vesicular staining pattern for internalized insulin in rat hepatocytes that colocalized partially with CD. In vivo pepstatin A treatment was without any observable effect on the insulin receptor content of endosomes but augmented the phosphotyrosine content of the endosomal insulin receptor after insulin injection. These results suggest that CD is the endosomal acidic insulinase activity which catalyzes the rate-limiting step of the in vivo cleavage at the PheB24-PheB25 bond, generating the inactive A1-21-B1-24 insulin intermediate.

REGISTRY NUMBERS: 9025-26-7: cathepsin D
DESCRIPTORS:
MAJOR CONCEPTS: Digestive System--Ingestion and Assimilation; Enzymology --Biochemistry and Molecular Biophysics; Methods and Techniques
BIOSYSTEMATIC NAMES: Muridae--Rodentia, Mammalia, Vertebrata, Chordata, Animalia
ORGANISMS: Sprague-Dawley rat (Muridae)--male
ORGANISMS: PARTS ETC: hepatic parenchymal cells--digestive system, endosomal compartment; liver--digestive system
COMMON TAXONOMIC TERMS: Animals; Chordates; Mammals; Nonhuman Vertebrates ; Nonhuman Mammals; Rodents; Vertebrates
CHEMICALS & BIOCHEMICALS: cathepsin D--analysis, *aspartic acid protease*, endosomal acidic insulinase, insulin endosomal processing role; insulin A chain--analysis, endosomal proteolysis, separation; insulin B chain--analysis, endosomal proteolysis, separation; internalized insulin--B chain carboxyl-terminal region, analysis, endosomal proteolysis, receptor-mediated degradation, separation
METHODS & EQUIPMENT: Beckman Coulter System Gold model 127 liquid chromatograph--Beckman Coulter, laboratory equipment; gel filtration TSK-GEL G3000 SWXL high-performance liquid chromatography column--Tosoh Corp., laboratory equipment; gel-filtration high performance liquid chromatography--Chromatographic Techniques, separation method; immunoblotting--Immunologic Techniques, detection method; immunofluorescence--Immunologic Techniques, detection method; immunoprecipitation--isolation method, precipitation; reverse-phase high performance liquid chromatography (RP-HPLC)--Chromatographic Techniques, separation method
CONCEPT CODES:
02506 Cytology - Animal
10802 Enzymes - General and comparative studies: coenzymes
14004 Digestive system - Physiology and biochemistry
BIOSYSTEMATIC CODES:
86375 Muridae

2/9/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012903989 BIOSIS NO.: 200100075828
Functional analysis of beta-secretase using mutagenesis and structural homology modeling
AUTHOR: McConlogue L C (Reprint); Agard D A; Ota M; Sinha S; Anderson J;

Basi G; Jacobson-Croak K; Chilcote T; Tatsuno G
AUTHOR ADDRESS: Elan Pharmaceuticals, S San Francisco, CA, USA**USA
JOURNAL: Society for Neuroscience Abstracts 26 (1-2): pAbstract No.-14.2 2000 2000
MEDIUM: print
CONFERENCE/MEETING: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000; 20001104
SPONSOR: Society for Neuroscience
ISSN: 0190-5295
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Proteolytc processing of the amyloid precursor protein by beta and gamma secretases leads to the formation Abeta peptide, the major component of Alzheimer''s disease plaques. The purification and cloning of betasecretase indicates that it is a novel aspartic acid protease. betasecretase is rate-limiting for the production of Abeta and therefore is an excellent target for therapeutic intervention in AD. Here we describe mutagenesis and homology modeling of betasecretase to investigate functional and structural aspects of this protein. Mutagenesis of both putative active site aspartates, led to overexpression of inactive enzyme which was correctly processed from the pro-enzyme to the mature enzyme as determined by amino acid sequencing. Over-expression of these mutants did not reduce endogenous betasecretase activity. Based on the homology of betasecretase sequence to related aspartic acid proteases, some conserved cysteine residues are missing and novel cysteine residues are found. C278, C380, C330 are conserved with C330 predicted by homology to form a disulfide bond with C380. We have generated a structural model based on the crystal structure of Atlantic cod pepsin. C216 and C420 are novel cysteines that based on the modeled structure are close enough to be involved in disulfide bonding. Cysteines at positions 216, 278, 330, 380, 420 were replaced with alanines by mutagenesis and enzymatic assay of expressed protein showed that all of these cysteines are required for optimal betasecretase enzymatic activity.

REGISTRY NUMBERS: 158736-49-3: beta-secretase; 9001-75-6: pepsin
DESCRIPTORS:
MAJOR CONCEPTS: Enzymology--Biochemistry and Molecular Biophysics; Nervous System--Neural Coordination
BIOSYSTEMATIC NAMES: Osteichthyes--Pisces, Vertebrata, Chordata, Animalia
ORGANISMS: Atlantic cod (Osteichthyes)
COMMON TAXONOMIC TERMS: Animals; Chordates; Fish; Nonhuman Vertebrates; Vertebrates
DISEASES: Alzheimer's disease--behavioral and mental disorders, nervous system disease
MESH TERMS: Alzheimer Disease (MeSH)
CHEMICALS & BIOCHEMICALS: amyloid beta-peptide--proteolytic processing; amyloid precursor protein--proteolytic processing; beta-secretase--*aspartic acid protease*, functional analysis; pepsin
METHODS & EQUIPMENT: amino acid sequencing--sequencing method
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Abstract
CONCEPT CODES:
10802 Enzymes - General and comparative studies: coenzymes
00520 General biology - Symposia, transactions and proceedings
10064 Biochemistry studies - Proteins, peptides and amino acids
20504 Nervous system - Physiology and biochemistry
20506 Nervous system - Pathology
BIOSYSTEMATIC CODES:

85206 Osteichthyes

2/9/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0012028708 BIOSIS NO.: 199900288368
HTLV-I protease, reverse transcriptase, and integrase: The viral enzymes of replication
AUTHOR: Ikeda Richard A (Reprint); Ding Y Shirley (Reprint); Ha Julie (Reprint); Lal Renu B; Owen S Michele
AUTHOR ADDRESS: School of Chemistry and Biochemistry, Georgia Institute of Technology, Atlanta, GA, 30332-0400, USA**USA
JOURNAL: Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology 20 (4): pA18 April 4, 1999 1999
MEDIUM: print
CONFERENCE/MEETING: Ninth International Conference on Human Retrovirology HTLV and Related Viruses Kagoshima, Japan April 5-9, 1999; 19990405
ISSN: 1077-9450
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 52350-85-3: integrase; 9068-38-6: reverse transcriptase
DESCRIPTORS:
MAJOR CONCEPTS: Enzymology--Biochemistry and Molecular Biophysics
CHEMICALS & BIOCHEMICALS: *aspartic acid protease*; integrase; reverse transcriptase; simian sarcoma virus reverse transcriptase; Gibbon ape leukemia virus reverse transcriptase; HTLV-I protease {human T-cell leukemia virus type I protease}--characterization, cloning; HTLV-I proteins--characterization, cloning
MISCELLANEOUS TERMS: Meeting Abstract; Meeting Abstract
CONCEPT CODES:
33506 Virology - Animal host viruses
10808 Enzymes - Physiological studies
00520 General biology - Symposia, transactions and proceedings

2/9/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011963044 BIOSIS NO.: 199900222704
Solid-phace synthesis of potential aspartic acid protease inhibitors containing a hydroxyethylamine isostere
AUTHOR: Zhou Jinglan (Reprint); Termin Andreas; Wayland Melissa; Tarby Christine M
AUTHOR ADDRESS: Department of Medicinal Chemistry, CombiChem, Inc., 9050 Camino Santa Fe, San Diego, CA, 92121, USA**USA
JOURNAL: Tetrahedron Letters 40 (14): p2729-2732 April 2, 1999 1999
MEDIUM: print
ISSN: 0040-4039
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A series of 1,3-diamino-2-propanol derivatives have been synthesized on solid phase as potential aspartic acid protease inhibitors. The developed methodology allows the incorporation of either

an alkyl group or H at the R2 site of hydroxyethylamine isostere.

DESCRIPTORS:
MAJOR CONCEPTS: Methods and Techniques; Pharmacology
CHEMICALS & BIOCHEMICALS: *aspartic acid protease*; 1,3-diamino-2-propanol derivatives--enzyme inhibitor, hydroxyethylamine isostere containing, protease inhibitor, synthesis
METHODS & EQUIPMENT: chemical synthesis protocol--synthetic method; solid-phase synthesis--synthetic method
MISCELLANEOUS TERMS: medicinal chemistry
CONCEPT CODES:
22002 Pharmacology - General
10050 Biochemistry methods - General
10502 Biophysics - General
38506 Chemotherapy - Antiviral agents
10802 Enzymes - General and comparative studies: coenzymes

2/9/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011093292 BIOSIS NO.: 199799727352
Discovery of antifungal agents from natural sources: Virulence factor targets
AUTHOR: Clark Alice M; Walker Larry A
AUTHOR ADDRESS: Natl. Cent. Dev. Natural Products, Dep. Pharmacognosy, Univ. Mississippi Sch. Pharmacy, University, MS 38677, USA**USA
JOURNAL: Abstracts of Papers American Chemical Society 214 (1-2): pAGRO 123 1997 1997
CONFERENCE/MEETING: 214th American Chemical Society National Meeting Las Vegas, Nevada, USA September 7-11, 1997; 19970907
ISSN: 0065-7727
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 9002-10-2: PHENOLOXIDASE
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Enzymology--Biochemistry and Molecular Biophysics; Pharmacognosy--Pharmacology; Pharmacology
BIOSYSTEMATIC NAMES: Fungi Imperfecti or Deuteromycetes--Fungi, Plantae
ORGANISMS: Candida sp. (Fungi Imperfecti or Deuteromycetes); Cryptococcus neoformans (Fungi Imperfecti or Deuteromycetes)
COMMON TAXONOMIC TERMS: Fungi; Microorganisms; Nonvascular Plants; Plants
CHEMICALS & BIOCHEMICALS: PHENOLOXIDASE
MISCELLANEOUS TERMS: ACTIVITY; ANTIFUNGAL AGENTS; *ASPARTIC ACID PROTEASE*; BIOCHEMISTRY AND BIOPHYSICS; PHARMACOGNOSY; PHENOLOXIDASE; SECRETION; VIRULENCE FACTOR TARGETS; Meeting Abstract
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
10060 Biochemistry studies - General
10502 Biophysics - General
22002 Pharmacology - General
38502 Chemotherapy - General, methods and metabolism
51518 Plant physiology - Enzymes
51522 Plant physiology - Chemical constituents
54000 Pharmacognosy and pharmaceutical botany
BIOSYSTEMATIC CODES:

15500 Fungi Imperfecti or Deuteromycetes

2/9/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0011084276 BIOSIS NO.: 199799718336
The design and synthesis of nonpeptide peptidomimetics: From neuropeptide hormone agonists and antagonists to inhibitors of aspartic acid proteases
AUTHOR: Smith Amos B Iii
AUTHOR ADDRESS: Dep. Chem., Univ. Pa., Philadelphia, PA 19104, USA**USA
JOURNAL: FASEB Journal 11 (9): pA831 1997 1997
CONFERENCE/MEETING: 17th International Congress of Biochemistry and Molecular Biology in conjunction with the Annual Meeting of the American Society for Biochemistry and Molecular Biology San Francisco, California, USA August 24-29, 1997; 19970824
ISSN: 0892-6638
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 38916-34-6Q: SOMATOSTATIN; 51110-01-1Q: SOMATOSTATIN; 33507-63-0: SUBSTANCE P
DESCRIPTORS:
MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Metabolism
CHEMICALS & BIOCHEMICALS: SOMATOSTATIN; SUBSTANCE P
MISCELLANEOUS TERMS: AMINO ACID; *ASPARTIC ACID PROTEASE*; BIOCHEMISTRY AND BIOPHYSICS; DESIGN; NONPEPTIDE PEPTIDOMIMETICS; PEPTIDE; SOMATOSTATIN; SUBSTANCE P; SYNTHESIS; TRISPYRROLINONE 1; Meeting Abstract
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
10060 Biochemistry studies - General
13002 Metabolism - General metabolism and metabolic pathways

2/9/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0010863164 BIOSIS NO.: 199799497224
Design and synthesis of pyrrolinone based non-peptidal peptidomimetics: From beta-sheet mimetics to an orally active HIV-1 protease inhibitor
AUTHOR: Smith Amos B Iii (Reprint); Favor David A (Reprint); Guzman Mark C (Reprint); Pasternak Alexander (Reprint); Benowitz Andrew B (Reprint); Huff Joel R; Kuo Lawerance; Darke Paul L; Chen Zhongguo; Emini Emilio A; Sprengeler Paul A (Reprint); Hirschmann Ralph (Reprint)
AUTHOR ADDRESS: Dep. Chem., Univ. Pennsylvania, Philadelphia, PA 19104, USA **USA
JOURNAL: Abstracts of Papers American Chemical Society 213 (1-3): pORGN 51 1997 1997
CONFERENCE/MEETING: 213th National Meeting of the American Chemical Society San Francisco, California, USA April 13-17, 1997; 19970413
ISSN: 0065-7727
DOCUMENT TYPE: Meeting; Meeting Abstract
RECORD TYPE: Citation
LANGUAGE: English
REGISTRY NUMBERS: 37205-61-1: PROTEASE INHIBITOR
DESCRIPTORS:

MAJOR CONCEPTS: Biochemistry and Molecular Biophysics; Enzymology--Biochemistry and Molecular Biophysics; Methods and Techniques; Microbiology
BIOSYSTEMATIC NAMES: Retroviridae--DNA and RNA Reverse Transcribing Viruses, Viruses, Microorganisms
ORGANISMS: human immunodeficiency virus type 1 (Retroviridae)
COMMON TAXONOMIC TERMS: DNA and RNA Reverse Transcribing Viruses; Microorganisms; Viruses
CHEMICALS & BIOCHEMICALS: PROTEASE INHIBITOR
MISCELLANEOUS TERMS: *ASPARTIC ACID PROTEASE*; BETA-SHEET MIMETICS; BIOCHEMISTRY AND BIOPHYSICS; CHEMICAL SYNTHESIS; ENZYME INHIBITOR SYNTHESIS; METHODOLOGY; SYNTHETIC METHOD; X-RAY STRUCTURE; 3,5-LINKED POLYPYRROLINONES; Meeting Abstract
CONCEPT CODES:
00520 General biology - Symposia, transactions and proceedings
10050 Biochemistry methods - General
10504 Biophysics - Methods and techniques
10506 Biophysics - Molecular properties and macromolecules
10806 Enzymes - Chemical and physical
33506 Virology - Animal host viruses
BIOSYSTEMATIC CODES:
03305 Retroviridae

2/9/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

0010225768 BIOSIS NO.: 199698693601
The inhibitory effects of the cysteine protease inhibitor, oryzacystatin, on digestive proteases and on larval survival and development of the southern corn rootworm (Diabrotica undecimpunctata howardi)
AUTHOR: Edmonds Heather S; Gatehouse Laurence N; Hilder Vaughan A; Gatehouse John A
AUTHOR ADDRESS: Dep. Biol. Sci., Univ. Durham, South Rd., DH1 3LE, UK**UK
JOURNAL: Entomologia Experimentalis et Applicata 78 (1): p83-94 1996 1996
ISSN: 0013-8703
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: At least eight proteolytic activities have been identified in the midgut contents of larval Southern corn rootworm (Diabrotica undecimpunctata howardi). Around 70% of protease activity could be arrested by the cysteine protease inhibitors E-64 and chicken egg-white cystatin, while the aspartic acid protease inhibitor pepstatin caused 30% inhibition. The cysteine protease activity was found to be highly sensitive to inhibition by both chicken egg-white cystatin and the rice cystatin, oryzacystatin 1. Oryzacystatin 1. expressed as a fully functional fusion protein in E. coli, was found to strongly inhibit larval gut protease activity. This recombinant oryzacystatin, incorporated into artificial diet at concentrations of 10 mM and above, caused significant decreases in larval survival and weight gain. E-64 was also shown to cause a significant antimetabolic in vivo effect. These results demonstrate the great potential for cysteine protease inhibitors, such as oryzacystatin, as tools for exploitation in the control of the Southern corn rootworm.

REGISTRY NUMBERS: 37353-41-6: CYSTEINE PROTEASE; 121273-67-4: ORYZACYSTATIN

; 9014-01-1: PROTEASES; 81989-95-9: CYSTATIN; 26305-03-3Q: PEPSTATIN; 39324-30-6Q: PEPSTATIN
DESCRIPTORS:
MAJOR CONCEPTS: Development; Digestive System--Ingestion and Assimilation ; Economic Entomology; Enzymology--Biochemistry and Molecular Biophysics; Metabolism; Pest Assessment Control and Management; Physiology
BIOSYSTEMATIC NAMES: Coleoptera--Insecta, Arthropoda, Invertebrata, Animalia; Lepidoptera--Insecta, Arthropoda, Invertebrata, Animalia
ORGANISMS: Diabrotica undecimpunctata howardi (Coleoptera); Lepidoptera (Lepidoptera)
COMMON TAXONOMIC TERMS: Animals; Arthropods; Insects; Invertebrates
CHEMICALS & BIOCHEMICALS: CYSTEINE PROTEASE; ORYZACYSTATIN; PROTEASES; CYSTATIN; PEPSTATIN
MISCELLANEOUS TERMS: ANTIMETABOLIC EFFECT; *ASPARTIC ACID PROTEASE INHIBITOR*; CYSTATIN; PEPSTATIN; PEST CONTROL; WEIGHT GAIN
CONCEPT CODES:
10060 Biochemistry studies - General
10064 Biochemistry studies - Proteins, peptides and amino acids
10808 Enzymes - Physiological studies
13002 Metabolism - General metabolism and metabolic pathways
14006 Digestive system - Pathology
25508 Development and Embryology - Morphogenesis
54600 Pest control: general, pesticides and herbicides
60004 Economic entomology - Field, flower and truck crops
60016 Economic entomology - Chemical
64076 Invertebrata: comparative, experimental morphology, physiology and pathology - Insecta: physiology
BIOSYSTEMATIC CODES:
75304 Coleoptera
75330 Lepidoptera

2/9/11 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

13026069 EMBASE No: 2005086563
Overexpression of PCSK9 accelerates the degradation of the LDLR in a post-endoplasmic reticulum compartment
Maxwell K.N.; Fisher E.A.; Breslow J.L.
J.L. Breslow, Lab. of Biochem. Genet. and Metab., Rockefeller University, Box 179, 1230 York Avenue, New York, NY 10021 United States
AUTHOR EMAIL: breslow@rockefeller.edu
Proceedings of the National Academy of Sciences of the United States of America (PROC. NATL. ACAD. SCI. U. S. A.) (United States) 08 FEB 2005 , 102/6 (2069-2074)
CODEN: PNASA ISSN: 0027-8424
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 56

Proprotein convertase subtilisin kexin 9 (PCSK9) is a member of the subtilisin serine protease family with an important role in cholesterol metabolism. PCSK9 expression is regulated by dietary cholesterol in mice and cellular sterol levels in cell culture via the sterol regulatory element binding protein transcription factors, and mutations in PCSK9 are associated with a form of autosomal dominant hypercholesterolemia. Overexpression of PCSK9 in mice leads to increased total and low-density

lipoprotein (LDL) cholesterol levels because of a decrease in hepatic LDL receptor (LDLR) protein with normal mRNA levels. To study the mechanism, PCSK9 was overexpressed in human hepatoma cells, HepG2, by adenovirus. Overexpression of PCSK9 in HepG2 cells caused a decrease in whole-cell and cell-surface LDLR levels. PCSK9 Overexpression had no effect on LDLR synthesis but caused a dramatic increase in the degradation of the mature LDLR and a lesser increase in the degradation of the precursor LDLR. In contrast, overexpression of a catalytically inactive mutant PCSK9 prevented the degradation of the mature LDLR; whereas increased degradation of the precursor LDLR still occurred. The PCSK9-induced degradation of the LDLR was not affected by inhibitors of the proteasome, lysosomal cysteine proteases, aspartic acid proteases, or metalloproteases. The PCSK9-induced degradation of the LDLR was shown to require transport out of the endoplasmic reticulum. These results indicate that overexpression of PCSK9 induces the degradation of the LDLR by a nonproteasomal mechanism in a post-endoplasmic reticulum compartment.

DRUG DESCRIPTORS:
*serine proteinase; *low density lipoprotein receptor
sterol regulatory element binding protein; proteasome inhibitor; cysteine proteinase inhibitor; proteinase inhibitor; metalloproteinase inhibitor; unclassified drug
MEDICAL DESCRIPTORS:
*protein degradation; *hypercholesterolemia
endoplasmic reticulum; cholesterol metabolism; protein expression; cholesterol intake; cell culture; autosomal dominant disorder; cell strain HepG2; adenovirus vector; cell surface; protein synthesis; protein transport; human; controlled study; human cell; article; priority journal
DRUG TERMS (UNCONTROLLED): proprotein convertase subtilisin kexin 9; *aspartic acid protease inhibitor*
CAS REGISTRY NO.: 37259-58-8 (serine proteinase); 37205-61-1 (proteinase inhibitor)
SECTION HEADINGS:
029 Clinical and Experimental Biochemistry

2/9/12 (Item 1 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

11468686 Genuine Article#: 657JW Number of References: 30
Title: Differential regulation by ambient pH of putative virulence factor secretion by the phytopathogenic fungus Botrytis cinerea
Author(s): Manteau S; Abouna S; Lambert B; Legendre L (REPRINT)
Corporate Source: Univ Western Sydney,Ctr Hort & Plant Sci,Penrith/NSW 1797/Australia/ (REPRINT); Univ Western Sydney,Ctr Hort & Plant Sci,Penrith/NSW 1797/Australia/; Univ Reims,Lab Plant Biol & Physiol, Plant Biochem & Mol Biol Res Unit, URVVC EA 2069,F-51687 Reims 2//France/
Journal: FEMS MICROBIOLOGY ECOLOGY, 2003, V43, N3 (APR 1), P359-366
ISSN: 0168-6496 Publication date: 20030401
Publisher: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS
Language: English Document Type: ARTICLE
Geographic Location: Australia; France
Journal Subject Category: MICROBIOLOGY
Abstract: The fungal pathogen Botrytis cinerea is capable of developing on a wide variety of host plants that differ greatly in their pH values and biochemical defences. To evaluate whether the pH of the host tissue can regulate the production of pathogenicity factors by this fungus, we

examined the ability of two isolates of B. cinerea that originated from different plant species to secrete putative virulence elements on synthetic media buffered at pH 2.0 to pH 7.0. Even though differing in the intensity of their responses, both isolates reacted similarly to their ambient pH. The production of extracellular polysaccharides and oxalic acid was detectable above pH 4.0 and pH 5.0 respectively. Conversely, the production of aspartic acid proteases could only be seen between pH 3.0 and 4.0. Finally, the secretion of polygalacturonase and laccase activity was found to exhibit two maxima, one around pH 3.1 and one around pH 6.0. Thus, pathogenicity factor production was found to be minimal between pH 4.5 and 5.5 and a different set of factors was produced at pH 3.1 and 6.0, two values that were found to correspond respectively to the average host fruit and leaf pH. These results demonstrate that ambient pH differentially regulates the synthesis of pathogenicity factors by Botrytis and may act as a novel regulatory element to assist this fungus in tuning its virulence machinery to the composition of its host tissue. (C) 2002 Published by Elsevier Science B.V. on behalf of the Federation of European Microbiological Societies.

Descriptors--Author Keywords: Botrytis cinerea ; laccase ; polygalacturonase ; *aspartic acid protease ;* oxalic acid ; pH

Identifiers--KeyWord Plus(R): GENE-EXPRESSION; ASPERGILLUS-NIDULANS; TRANSCRIPTION FACTOR; ENVIRONMENTAL PH; CANDIDA-ALBICANS; ACID; INDUCTION; GROWTH; ACTIVATION; BERRIES

Cited References:

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JONES LJ, 1997, V251, P144, ANAL BIOCHEM
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NAIR NG, 1993, V97, P1012, MYCOL RES
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SLOMCZYNSKI D, 1995, V61, P907, APPL ENVIRON MICROB
STAPLES RC, 1995, V134, P1, FEMS MICROBIOL LETT
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VERHOEFF K, 1988, V122, P327, J PHYTOPATHOL
WATSON N, 1992, V174, P530, J BACTERIOL
WUBBEN JP, 2000, V37, P152, CURR GENET
YAKOBY N, 2000, V66, P1026, APPL ENVIRON MICROB

2/9/13 (Item 2 from file: 34)

DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

07557483 Genuine Article#: 180UM Number of References: 16
Title: Solid-phase synthesis of potential aspartic acid protease inhibitors containing a hydroxyethylamine isostere
Author(s): Zhou JL (REPRINT) ; Termin A; Wayland M; Tarby CM
Corporate Source: COMBICHEM INC,DEPT MED CHEM, 9050 CAMINO SANTA FE/SAN DIEGO//CA/92121 (REPRINT)
Journal: TETRAHEDRON LETTERS, 1999, V40, N14 (APR 2), P2729-2732
ISSN: 0040-4039 Publication date: 19990402
Publisher: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND
Language: English Document Type: ARTICLE
Geographic Location: USA
Subfile: CC PHYS--Current Contents, Physical, Chemical & Earth Sciences; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: CHEMISTRY, ORGANIC
Abstract: A series of 1,3-diamino-2-propanol derivatives have been synthesized on solid phase as potential aspartic acid protease inhibitors. The developed methodology allows the incorporation of either an alkyl group or H at the R-2 site of hydroxyethylamine isostere. (C) 1999 Elsevier Science Ltd. All rights reserved.
Descriptors--Author Keywords: *aspartic acid protease ;* inhibitors ; hydroxyethylamine isostere ; solid-phase synthesis
Identifiers--KeyWord Plus(R): HIV PROTEASE
Cited References:
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2/9/14 (Item 3 from file: 34)
DIALOG(R)File 34:SciSearch(R) Cited Ref Sci

04901284 Genuine Article#: UQ420 Number of References: 31
Title: THE PRIMARY STRUCTURE AND ENZYMATIC-PROPERTIES OF PORCINE PROCHYMOSIN AND CHYMOSIN
Author(s): HOUEN G; MADSEN MT; HARLOW KW; LONBLAD P; FOLTMANN B
Corporate Source: STATENS SERUM INST,DEPT AUTOIMMUNOL,ARTILLERIVEJ 5/DK-2300 COPENHAGEN S//DENMARK/; UNIV COPENHAGEN,DEPT PROT CHEM/DK-1353 COPENHAGEN K//DENMARK/
Journal: INTERNATIONAL JOURNAL OF BIOCHEMISTRY & CELL BIOLOGY, 1996, V28, N6 (JUN), P667-675
ISSN: 1357-2725
Language: ENGLISH Document Type: ARTICLE

Geographic Location: DENMARK
Subfile: SciSearch; CC LIFE--Current Contents, Life Sciences
Journal Subject Category: BIOCHEMISTRY & MOLECULAR BIOLOGY; CELL BIOLOGY
Abstract: Preliminary investigations by N-terminal sequence analysis showed that pig and calf chymosin possessed 80% amino acid sequence identity but showed considerable differences in their enzymatic properties. A comparison of their structures may therefore contribute to an understanding of the significance of the amino acid residues responsible for the differences in these properties. Pig chymosis was extracted from the stomachs of pigs of less than 3 weeks of age, and was purified by ion exchange chromatography. Half of the primary structure was determined by amino acid sequencing and the complete structure was deduced from a cloned chymosin cDNA. Results showed that the zymogen showed 81% sequence identity with calf prochymosin and 57% identity with pig pepsinogen A. The size of the propart and location of the residue which becomes the N-terminus in the active molecule were the same in the prochymosins. The maximum general proteolytic activity at pH 3.5 of pig chymosin was 2-3% of that of the activity of pig pepsin A at pH 2, whereas the milk clotting activity relative to the general proteolytic activity of pig chymosin was much higher than that of calf chymosin. Agar gel electrophoresis at pH 5.3 of stomach extracts of individual pigs showed the existence of two predominant genetic variants of zymogen and enzyme. The two variants could not be distinguished by amino acid composition or N-terminal sequencing, and no differences in the enzymatic properties of the genetic variants were observed. It was concluded that of the residues that participate in the substrate binding, calf and pig chymosin differ in the following positions (pig pepsin numbering, subsites in parentheses): Ser 12 Thr (S-4), Leu 30 Val (S-1/S-3), His 74 Gln (S'(2)), Val 111 Re (S-1/S-3), Lys 220 Met (S-4). With regard to the low general proteolytic activity of pig chymosin, the substitution Asp 303 Val relative to calf chymosin may contribute to an explanation of this. (C) 1996 Elsevier Science Ltd
Descriptors--Author Keywords: PROCHYMOSIN ; *ASPARTIC ACID PROTEASE ; *PIG ; CDNA ; PRIMARY STRUCTURE
Identifiers--KeyWords Plus: POLYACRYLAMIDE-GEL ELECTROPHORESIS; MOLECULAR-CLONING; PROTEINS; PEPSIN; MUTAGENESIS; RESOLUTION; PROTEASES; MEMBRANES; SEQUENCE; PIGS
Research Fronts: 94-3070 001 (RAT SKELETAL-MUSCLE; DEVELOPMENTAL REGULATION; YEAST SACCHAROMYCES-CEREVISIAE)
94-4806 001 (GENE ORGANIZATION; LONG-CHAIN FATTY-ACID TRANSPORT; TRANSCRIPTION FACTOR)
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2/9/15 (Item 1 from file: 71)

00487022 96180987

HIV protease and the pathogenesis of AIDS

Goldberg B.; Stricker R.B.
ADDRESS: Dr. R.B. Stricker, 450 Sutter Street, San Francisco, CA 94108, United States

Journal: Research in Virology, 147/6 (375-379), 1996, France
PUBLICATION DATE: 19960000
CODEN: RESVE
ISSN: 0923-2516
DOCUMENT TYPE: Short Survey
LANGUAGES: English SUMMARY LANGUAGES: French

DESCRIPTORS:
AIDS; HIV; Protease; *Aspartic acid protease*; Protease inhibitors; Pathogenesis; Hypothesis

CLASSIFICATION CODE AND DESCRIPTION:
86.7.7.4 - IMMUNOLOGY AND INFECTIOUS DISEASES / IMMUNITY TO INFECTION / AIDS and HIV / Pathogenesis and syndrome manifestations
82.8.3 - PROTEIN BIOCHEMISTRY / HYDROLYTIC ENZYMES (EC 3.) / Proteases, Peptidases and Proteinases
82.12.7.4 - PROTEIN BIOCHEMISTRY / OTHER PROTEINS / Microbial Proteins / Viral
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PICKS is set ON as an alias for
5,159,143,358,340,344,348,447,73,155,349,266,10,34,434,42,43,50,65,71,91,94,14
4,198,304,370,467,444,357,156,157.
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SYSTEM:HOME
Cost is in DialUnits
Menu System II: D2 version 1.7.9 term=ASCII
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     $0.06  Estimated total session cost   0.213 DialUnits


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Set	Items	Description
S1	1	ASPARTIC ENZYME

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1/9/1 (Item 1 from file: 5)

0013972220 BIOSIS NO.: 200200565731

Comparative digestive enzyme ontogeny in two marine larval fishes: Pacific threadfin (Polydactylus sexfilis) and bluefin trevally (Caranx melampygus)

AUTHOR: Kim Bong G; Divakaran S; Brown Christopher L (Reprint); Ostrowski Anthony C
AUTHOR ADDRESS: Marine Biology Program, Florida International University, 3000 NE 151st St., North Miami Beach, FL, 33181, USA**USA

JOURNAL: Fish Physiology and Biochemistry 24 (3): p225-241 April, 2001 2001
MEDIUM: print
ISSN: 0920-1742
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The specific activity of digestive enzymes; aspartic and serine protease, collagenase, lipase, acid and alkaline amylase, acid and alkaline phosphatase, and chitinase was assayed throughout early development in two species of marine fishes: the Pacific threadfin (Polydactylus sexfilis) and bluefin trevally (Caranx melampygus). Specific enzyme activities were determined on whole larval extracts sampled at selected stages of development, from day 0 to day 30 post-hatching. Similar developmental patterns of enzyme specific activity were observed in the two species, although differences in timing, amplitude and effects of first feeding were noted. Amylase activity increased prior to first feeding, peaking at the middle of the larval period, and becoming nearly undetectable by the time of larval-to-juvenile metamorphosis. Serine protease, collagenase, lipase and alkaline (and acid for threadfin) phosphatase activities increased gradually, followed by sharp increases to a plateau during the second half of larval development. Aspartic protease and chitinase activities, in addition to acid phosphatase (for trevally), were low to undetectable in the first half of development, increasing through metamorphosis. In the trevally only, this group of enzymes exhibited high activity levels at the time of hatching, followed by a precipitous drop. Species-dependent differences in enzyme specific activity at first feeding may have been a result of differences in yolk utilization. These results, taken in the context of earlier reports, lead us to conclude that carbohydrate utilization may play a significant role in the earlier phases of development among some marine larvae, followed by a shift to protein and lipid utilization.

REGISTRY NUMBERS: 9001-77-8: acid phosphatase; 9001-78-9: alkaline phosphatase; 9001-06-3: chitinase; 9001-12-1: collagenase; 9001-62-1: lipase; 37259-58-8: serine protease
DESCRIPTORS:

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  MAJOR CONCEPTS: Digestive System--Ingestion and Assimilation; Enzymology
    --Biochemistry and Molecular Biophysics
  BIOSYSTEMATIC NAMES: Osteichthyes--Pisces, Vertebrata, Chordata, Animalia
  ORGANISMS: Caranx melampygus (bluefin trevally) (Osteichthyes);
    Polydactylus sexfilis (Pacific threadfin) (Osteichthyes)
  COMMON TAXONOMIC TERMS: Animals; Chordates; Fish; Nonhuman Vertebrates;
    Vertebrates
  CHEMICALS & BIOCHEMICALS:   acid phosphatase; alkaline amylase; alkaline
    phosphatase; *aspartic enzyme*--digestive enzyme; chitinase;
    collagenase; lipase; serine protease--digestive enzyme
  METHODS & EQUIPMENT: carbohydrate utilization assay--analytical method
  MISCELLANEOUS TERMS:   digestive enzyme ontogeny; larval-to-juvenile
    metamorphosis
CONCEPT CODES:
  10802 Enzymes - General and comparative studies: coenzymes
  14004 Digestive system - Physiology and biochemistry
BIOSYSTEMATIC CODES:
  85206 Osteichthyes
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Set     Items   Description
S1          1   ASPARTIC ENZYME
S2   12894427   D
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